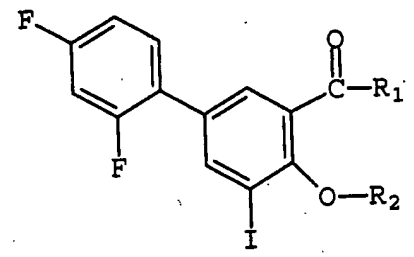
CLAIMS

1. A compound of structural formula (I):



(I)

in which

R_1 is a $-NR_aR_b$ group, where R_a and R_b, independently, are a hydrogen atom or a C_1-C_6 alkyl group; $-OR_C$ group, where R_C is a hydrogen atom or a C_1-C_6 alkyl group; a glycosyl; a C_1-C_6 polyhydroxyalkyl; or a $-NH-CH(R_d)-COOR_e$ group, where R_d is a side chain of one of the 20 natural alpha-amino acids in either of their two enantiomerically pure forms L or D, and R_e is a hydrogen atom or a C_1-C_6 alkyl group; and

R_2 is a hydrogen atom, a C_1-C_6 alkyl group, a glycosyl; a C_1-C_6 polyhydroxyalkyl; $-C(=O)-R_f$ group, where R_f is a C_1-C_6 alkyl group; or a $-CH_2-COO-R_g$ group, where R_g is a hydrogen atom or a C_1-C_6 alkyl group;

and pharmaceutically acceptable salts thereof.

2. A compound according to claim 1, characterised in that R_1 is selected from: OH, NH_2, OMe, OEt, or a $CH(R_d)-COR_e$ group, where R_d is the side chain of glycine, alanine, leucine, valine, aspartic acid or asparagine and where R_e is H or a C_1-C_6 alkyl group; and R_2 is selected from: H, Me, glycosyl, a $-C(=O)-R_f$ group, where R_f is a Me, Et, t-Bu group; or a $-CH_2-COO-R_g$ group, where R_g is a hydrogen atom or a t-Bu group.

3. A compound according to claim 1, characterised in that it is selected from the following compounds:

[1] 5-(2,4-difluorophenyl)-3-iodo-salicylic acid;
[2] ethyl 5-(2,4-difluorophenyl)-3-iodo-salicylate;
[3] methyl 5-(2,4-difluorophenyl)-3-iodo-salicylate;
[4] 5-(2,4-difluorophenyl)-3-iodo-salicylamide;
[5] tert-butyl [2-aminocarbonyl-4-(2,4-difluorophenyl)-6-iodo-phenoxy]-acetate;
[6] [2-aminocarbonyl-4-(2,4-difluorophenyl)-6-iodo-phenoxy]acetic acid;
[7] 5-(2,4-difluorophenyl)-3-iodo-salicylic acid 1-O-β-glycoside;
[8] ethyl 2',4'-difluoro-4-methoxy-5-iodo-[1,1']biphenyl-3-carboxylate;
[9] 2',4'-difluoro-4-methoxy-5-iodo-[1,1']biphenyl-3-carboxylic acid;
[10] ethyl 2',4'-difluoro-4-acetyloxy-5-iodo-[1,1']biphenyl-3-carboxylate;
[11] 2',4'-difluoro-4-(*t*-butylcarbonyloxy)-5-iodo-[1,1']biphenyl-3-carboxylic acid;
[12] 2',4'-difluoro-4-(ethylcarbonyloxy)-5-iodo-[1,1']biphenyl-3-carboxylic acid;
[13] ethyl ester of N-[5-(2,4-difluorophenyl)-3-iodo-salicyloyl]glycine;
[14] N-[5-(2,4-difluorophenyl)-3-iodo-salicyloyl]glycine;
[15] N-[5-(2,4-difluorophenyl)-3-iodo-salicyloyl]alanine;
[16] N-[5-(2,4-difluorophenyl)-3-iodo-salicyloyl]leucine;
[17] N-[5-(2,4-difluorophenyl)-3-iodo-salicyloyl]serine;
[18] N-[5-(2,4-difluorophenyl)-3-iodo-salicyloyl]valine;
[19] N-[5-(2,4-difluorophenyl)-3-iodo-salicyloyl]-aspartic acid;
[20] N-[5-(2,4-difluorophenyl)-3-iodo-salicyloyl]asparagine.

4. A method for the preparation of a compound of formula (I) according to claims 1 characterised in that it comprises a step of reacting diflunisal or derivatives thereof with an iodination reagent.

5. A method according to claim 4 characterised in that the iodination reagent may be selected from: elemental iodine; iodide salts such as sodium iodide or potassium iodide; iodonium salts such as iodine chloride; iodonium complexes such as bis(pyridine)iodonium (I) tetrafluoroborate or bis(sym-collidine)iodonium (I) hexafluorophosphate; and organic iodine compounds such as iodobenzene diacetate or N-iodosuccinimide.

6. A pharmaceutical composition containing a compound according to

claims 1 and one or more pharmaceutically acceptable excipients.

7. A method of treatment of neurodegenerative diseases, including amyloid neurodegenerative diseases, Alzheimer's disease, Parkinson's disease, Huntington's disease, Creutzfeldt-Jakob disease, cystic fibrosis, late-onset diabetes, motor neuron disease, Mediterranean fever, Muckle-Wells syndrome, idiopathic myeoloma, amyloid cardiopathy, Down's syndrome, Kuru disease, Gerstmann-Straussler-Schienker syndrome, amyloid valvular deposits, amyloidosis in dialysis patients, inclusion body myositis, amyloid muscular deposits, Sickle Cell anemia, primary systemic amyloidosis, senile systemic amyloidosis, familial amyloid polyneuropathy I, familial amyloid polyneuropathy III, hereditary cerebral amyloid angiopathy, angiopathy-related amyloidosis, Finnish hereditary systemic amyloidosis, type II diabetes, medullar thyroid carcinoma, spongiform encephalopathy, atrial amyloidosis, hereditary non-neuropathic systemic amyloidosis, injection-localized amyloidosis, and hereditary renal amyloidosis comprising administration of a composition according to claim 6.

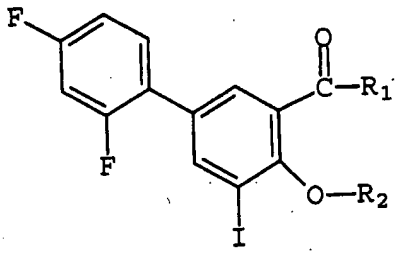
8. A method of treatment according to claim 7 for the treatment of familial amyloid polyneuropathy I and familial amyloid polyneuropathy III.

9. A method of treatment of rheumatoid arthritis, rheumatoid fever, osteoarthritis, musculoskeletal pains, inflammatory bowel disease, coronary artery diseases and postoperative deep vein thrombosis comprising administration of a composition according to claim 6.

SUMMARY

COMPOUNDS USEFUL FOR THE TREATMENT OF DISEASES ASSOCIATED WITH THE FORMATION OF AMYLOID FIBRILS

The present invention provides new amyloidogenesis inhibiting compounds of formula (I):



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R_2 is a hydrogen atom, a C_1-C_6 alkyl group, a glycosyl; a C_1-C_6 polyhydroxyalkyl; $-C(=O)-R_f$ group, where R_f is a C_1-C_6 alkyl group; or a $-CH_2-COO-R_g$ group, where R_g is a hydrogen atom or a C_1-C_6 alkyl group;

and pharmaceutically acceptable salts thereof, which are useful in the treatment of neurodegenerative diseases, among others.